What is the relationship between the intake of milk and milk products and bone health?

Conclusion

Moderate evidence indicates that the intake of milk and milk products is linked to improved bone health in children. Limited evidence suggests a positive relationship between the intake of milk and milk products and bone health in adults, but results are inconsistent due to variability in outcomes considered.

Grade: Moderate

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades, click here.

Evidence Summary Overview

Research since 2004 indicates that the intake of milk and milk products is linked to improved bone health in children. Results in adults are mixed. The conclusion reached for this question is based on a review of three systematic reviews or meta-analyses (Alvarez-Leon, 2006; Huncharek, 2008; Kanis, 2005), three primary research studies conducted since the reviews (Budek, 2007; Kristensen, 2005; McCabe, 2004), one longitudinal study (Rockell, 2005), one case-control study (Konstantynowicz, 2007) and one cross-sectional study (Al-Zahrani, 2006), all published since 2004.

The results of the systematic reviews and meta-analyses are inconsistent when children and adults are considered together. In a meta-analysis focused on children, Huncharek et al, (2008) examined the relationship between dairy and calcium intake and bone mineral content. Their review of 21 studies concluded that increased dairy/calcium intake, with or without vitamin D supplementation, results in significantly higher total body and lumbar spine bone mineral content among children with low baseline intakes of dairy, calcium, and/or vitamin D. In a small, short-term study among pre-pubertal boys consuming equal amounts of protein, Budek et al, (2007) found that a high intake of milk, but not meat, decreased bone turnover. However, the relevance of reduced turnover for peak bone mass is unclear.

A longitudinal study conducted in New Zealand (Rockell, 2005), assessed two-year changes in bone and body composition in young children with a history of prolonged milk avoidance. The authors concluded that young milk avoiders demonstrated persistent height reduction, overweight and osteopenia at the ultradistal radius and lumbar spine over two years of follow-up.

Alvarez-Leon et al, (2006) reviewed literature on the associations between the consumption of dairy products and health outcomes, including two review papers on bone health. They concluded that there is weak evidence of the protective capacity of dairy products on bone health, noting that limitations in studies examining this relationship make it difficult to make firm conclusions about the effect of dairy products on bone health.

Kanis et al, (2005) reviewed six prospectively studied cohorts from European, Australian and Canadian research. They examined calcium intake, measured by milk consumption, and its association with the risk of fracture. They found no significant relationship between low intake of

calcium and fracture risk. This study did not include other sources of dietary calcium besides milk and did not account for variations in vitamin D intake or sunlight exposure. Therefore, the authors caution that these findings should not be misinterpreted as suggesting that calcium is not causally related to fracture risk nor that calcium does not play a role in fracture prevention.

Results from three intervention studies supported the role of dairy products in bone health. McCabe et al, (2004) found that calcium supplementation protected study participants from bone loss and that higher dairy product consumption was associated with greater hip bone mineral density (BMD) in men, but not in women. In a small study of Caucasian males who replaced milk with cola beverages in their diet for 10 days, Kristensen et al, (2005) concluded that replacement of cola for milk results in a low calcium intake, which may negatively affect bone health.

In summary, these reviews support that calcium and milk and milk products play an important role in bone mineral content in children. Results from adult trials are mixed.

Evidence Summary Paragraphs

Systematic Reviews / Meta-Analyses:

Alvarez-Leon et al, 2006 (positive quality) systematically reviewed papers on the associations between consumption of dairy products and health outcomes, including cancer, bone health and cardiovascular disease. Relevant articles were obtained through searching the MEDLINE database (from 1966 to January 2005) using the search terms: 'Dairy products', defined as 'raw and processed or manufactured milk, and milk-derived products' including butter, cheese, ice cream, margarine and milk and cultured milk products (yoghurt). This search revealed 85,000 articles. After excluding studies, and including only meta-analyses and systematic reviews, the final sample consisted of 14 meta-analyses and systematic reviews. This final sample consisted of six papers on dairy products and cancer, six papers on dairy products and cardiovascular disease (CVD) and two papers on dairy products and bone health. Evidence from these papers was summarized and evaluated. Weinsier and Krumdieck (2000) reviewed 12 articles. Among the 12 articles, there were six that found no effect between the intake of dairy products and bone health, five found a positive effect and one found a negative effect. Women under 30 years seemed to gain the most benefit. Cumming and Nevitt (1997) found 14 studies that evaluated calcium (Ca) supplements (four randomized trials, three non-randomized trials and seven observational epidemiological studies) and 23 observational studies that evaluated dietary Ca (non-randomized trials). The main conclusion emphasized by the authors was that increased Ca intake among postmenopausal women appeared to be associated with a small reduction in risk of fracture, with about a 30% reduction in fracture risk among those taking higher amounts of Ca (1 g daily as a supplement). The authors concluded that there is weak evidence of a protective capacity of dairy products on bone health.

Huncharek et al, 2008 (positive quality) conducted a meta-analysis to determine the relationship between dairy and calcium intake and bone mineral content (BMC) in children. A search was done using the search terms bone/bones, dairy products, calcium and calcium/dietary to identify relevant studies published between 1966 and 2006. The search identified 1,200 studies, and after inclusion/exclusion criteria were applied, 21 studies with 3,821 subjects (83% female) ages four to 17.3 years were included in the meta-analysis. Data were pooled from randomized controlled trials (RCTs) and observational studies using the primary outcomes of summary mean difference BMC. Sensitivity analyses were employed to evaluate any observed statistical heterogeneity and to examine the influence of specific study characteristics on the summary estimate of effect. Combining data from 21 RCTs using total body bone mineral content (TB-BMC) as the outcome of interest, yielded a non-statistically significant increase in BMC of 2g (supplemented vs. controls). However, sensitivity tests revealed that baseline calcium intake could be accounting for the

statistical heterogeneity. Therefore, when results from three studies utilizing low intake subjects were pooled, increased dairy/calcium intake was significantly associated with a mean BMC increase of 49g. In addition, pooling data from two studies combining dairy/calcium and vitamin D supplementation showed a significant mean increase in lumbar spine BMC of 35g. These results suggest that increased dairy/calcium intake, with or without vitamin D supplementation, results in significantly higher total body and lumbar spine BMC among children with low baseline intakes of dairy, calcium and/or vitamin D.

Kanis et al, 2005 (positive quality) conducted a meta-analysis to quantify the fracture risk associated with a low dietary intake of milk and calcium, and to explore the dependence of this risk with age, sex and bone mineral density (BMD). Data from 39,563 adults (age range: 21-103 years) participating in six prospectivecohort studies in Europe, Australia and Canada were used for the meta-analysis. There was no significant (NS) relationship between low intake of calcium and hip fracture risk in either sex at any age. For osteoporotic fractures, a small, but significant risk was found from the age of 80 years (RR=1.15; 95% CI: 1.02-1.30); however this association was no longer significant when adjusted for BMD. There was a weak but significant correlation between intake of milk and BMD (r=0.03643, P=4.5 x 10-10). The authors concluded that the main finding of the present study was that a low intake of calcium, as judged by the intake of milk, does not confer a substantial increase in fracture risk. This study did not include other sources of dietary calcium besides milk, and did not account for variations in vitamin D intake or sunlight exposure. Therefore, the authors caution that these findings not be misinterpreted as suggesting no causative role of calcium in the causation of fractures, nor a role for calcium nutrition in their prevention.

Primary Research:

Trials:

Budek et al, 2007 (positive quality) conducted a non-randomized trial to compare the short-term effect of high milk and a high meat intake, identical in the amount of protein, on bone formation, bone resorption and weight in pre-pubertal boys. The study was conducted in Denmark. Male subjects (N=24, 12 per group) aged eight years participated in a seven-day trial. Subjects were instructed to consume either 1.5 liter of skimmed milk per day or 250 g of low-fat meat per day for seven days. Each treatment was designed to add approximately 53g of protein to the diet. Otherwise, subjects were instructed to maintain their normal dietary intake during the study. Three-day weighted food records (two weekdays and one weekend day) were kept for the three days preceding the intervention and for the last three days of the study. Measures of bone formation/resorption and weight were obtained between 8 and 10 a.m. on day zero (baseline) and day seven (end of intervention). At baseline, the groups did not differ with respect to serum concentrations of bone markers. After seven days, serum osteocalcin (s-OC) ($P<0.003$) and serum C-terminal telopeptides of type I collagen (s-CTX) ($P<0.04$) were significantly reduced in the milk group compared to the meat group. While serum bone-specific alkaline phosphate (s-BAP) decreased in both groups, there were no significant differences between the groups. Boys in the milk group increased body weight by 0.54kg compared with the boys in the meat group, that did not exhibit a change in body weight ($P=0.003$).

Kristensen et al, 2005 (neutral quality), a randomized crossover trial conducted in Denmark, investigated the short-term effects of replacing milk with cola beverages in young men on a low-calcium diet in order to study the effect on calcium homeostasis and bone turnover. 2.5 liters of either cola or semi-skimmed milk were consumed each day in two 10-day experimental periods separated by a 10-day washout period. During the two diet periods, the same low-calcium diet was given to the subjects; all meals were provided. 11 Caucasian males, aged 22-29 years, were enrolled

and completed the study. An increase in serum phosphate (P<0.001), 1,25(OH)2D (P<0.001), PTH (P=0.046) and osteocalcin (P<0.001) was observed in the cola period compared to the milk period and bone resorption was significantly increased following the cola period, seen as increased serum CTX (P<0.001) and urinary NTX (P<0.001) compared to the milk period. No changes were observed in serum concentrations of calcium or B-ALP. The authors concluded that the trend towards replacement of milk with cola and other soft drinks results in a low calcium intake, which may negatively affect bone health.

McCabe et al, 2004 (neutral quality) used both a RCT and a cross-sectional study to:

1. Examine the cross-sectional relationship between consumption of calcium and other nutrients from dairy products and bone mineral density (BMD) at the hip in elderly black and white men and women
2. Examine the impact of calcium supplement intake on the BMD loss in a longitudinal study of white men and women.

There were 289 white women and 116 white men who participated in the RCT, and their data was combined with data from 265 black women and 75 black men for the cross-sectional study; all subjects were ≥60 years of age. The study was conducted in the US. For the trial, subjects received daily placebo, 750 mg Ca per day or 15 microgram 25-hydroxyvitamin D_3 per day for four years. For all subjects dietary intake data was collected using the National Cancer Institute's Health Habits and History questionnaire, and bone mineral density was assessed using dual energy X-ray absorptiometry (DEXA). For all participants, average total calcium intake from dairy was 436±289mg, with an additional 239±93mg coming from nondairy dietary sources. In the cross-sectional analysis, a partial positive correlation was found between total hip BMD and dairy calcium in men (P<0.05, r=0.23) but not in women (NS, r=0.02). The results of the RCT showed that the effect of calcium supplementation on femoral neck BMD depended on baseline dietary calcium intake (P<0.05). Those participants with deficient diets (<1.5 servings or <450mg Ca per day) at baseline who were treated with calcium had less change in femoral neck BMD compared to those treated with placebo. Also, the effect of calcium supplementation on femoral neck and hip BMD was evident in those that were less than 72 years old (P<0.05) at baseline, but not in those that were older than 72 years at baseline (NS). The authors concluded that the cross-sectional results indicated that higher dairy product consumption is associated with greater hip bone mineral density in men, but not in women, and that long-term calcium supplementation protected both men and women from bone loss in the longitudinal study.

Longitudinal Study:

Rockell et al, 2005 (positive quality), a longitudinal study conducted in New Zealand, assessed two-year changes in bone and body composition in young children with a history of prolonged milk avoidance. The baseline visit consisted of 50 Caucasian children aged three to 10 years; 28 girls and 18 boys (mean age 8.1±2.0 years) completed the follow-up study. Calcium intake was assessed by food-frequency questionnaire (FFQ), as well as four-day diet records. Bone mineral density (BMD) and body composition were measured using DEXA. Thirteen children (28.3%) had history of fracture; five new fractures had occurred during the two-year follow-up. At follow-up, calcium intakes were positively correlated with Z scores for total body bone mineral content (r=0.34, P<0.023), total bone area (r=0.33, P<0.025), ultradistal radial bone mineral density (r=0.36, P<0.014) and 33% radial BMD (r=0.30, P<0.045). Every additional 100mg of calcium consumed was commensurate with a change of approximately 0.1 unit of Z score for these measurements. However, although some catch-up in height had taken place during the follow-up, the group remained significantly shorter than the reference population, with elevated body mass index (BMI).

The authors concluded that young milk avoiders demonstrated persistent height reduction, overweight and osteopenia at the ultradistal radius and lumbar spine over two years of follow-up.

Case-Control Studies:

Konstantynowicz et al, 2007 (neutral quality), a case-control study conducted in Poland, examined the association between consumption of a milk-free diet and fracture risk, in 91 cases with fractures (57 boys and 34 girls, aged 2.5-20 years) and 273 age- and sex-matched controls without fractures (three per case, 171 boys and 102 girls). All children with cow's milk allergy were treated with a restrictive milk-free diet for 2.5 to 14 years. Weight, height, bone mineral density (BMD) and body composition were measured in all children, while calcium intake was assessed through 24-hour recall in a subset of 46 children. In girls, 29.4% of cases and 11.8% of controls had consumed a milk-free diet, producing an odds ratio (OR) for fracture associated with a milk-free diet of 4.6 (95% CI: 1.4, 15.5; P<0.01), while in boys, 23% of cases and 19% of controls had consumed a milk-free diet, producing an OR for fracture associated with a milk-free diet of 1.3 (95% CI: 0.6, 2.7; NS). No association was found between calcium intake, BMD or fracture prevalence in the sub-set of children, leading the authors to conclude that cow's milk allergy was associated with increased fracture risk in girls.

Cross-Sectional Study:

Al-Zahrani et al, 2006 (positive quality) conducted a cross-sectional study to examine whether or not there was an association between the intake of dairy products and periodontitis prevalence among adults (N=12,764; 6,549 females, 6,215 males) using National Health and Nutrition Examination Survey III (NHANES III) data. A 24-hour dietary recall collected information from participants regarding their intake of food and beverages (except for plain drinking water) for the past 24 hours, and the number of servings of dairy products was calculated. Mean intake of dairy products for the study was 2.1 servings per day. Rates of periodontitis were significantly lower among individuals in the highest quintile of dairy intake (11.2±1.1%) compared to those in the lowest quintile of dairy intake (17.8±1.3%; P<0.01). Individuals in the highest quintile of dairy intake were 41% less likely to have periodontitis than those in the lowest quintile (OR: 0.80; 95% CI: 0.61, 1.07; P<0.05) (adjusted for age, gender, race/ethnicity, smoking, education, diabetes, poverty index; vitamin use, BMI, physical activity, time since the last dental visit, gingival bleeding and dental calculus). The authors concluded that a strong inverse association between intake of dairy products and prevalence of periodontitis was present, even after controlling for major risk factors of periodontitis.

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Author, Year, Study Design, Class, Rating	Participants	Description of Study Design	Outcomes
Al-Zahrani MS, 2006 Study Design: Cross-sectional study	N=12,764 adults (6,549 females, 6,215 males) from NHANES III data. Location: United	Examined whether or not there was an association between the intake of dairy products and periodontitis	Rates of periodontitis were significantly ↓ among individuals in highest quintile of dairy intake (11.2±1.1%), compared to those in lowest quintile of

Class: D Rating:	States.	prevalence using NHANES III data. A 24-hour dietary recall collected information from participants regarding their intake of food and beverages.	dairy intake (17.8±1.3%; P<0.01). Individuals in highest quintile of dairy intake were 41% less likely to have periodontitis than those in the lowest quintile (OR: 0.80; 95% CI: 0.61, 1.07; P<0.05) (adjusted for age, gender, race/ethnicity, smoking, education, diabetes, poverty index; vitamin use, BMI, physical activity, time since the last dental visit, gingival bleeding and dental calculus).
Alvarez-León EE, Roman-Vinas B et al, 2006 Study Design: Meta-analysis or Systematic Review Class: M Rating:	N=14 meta-analyses and systematic reviews: • Six on dairy products and cancer. • Six on dairy products and CVD • Two on dairy products and bone health.	Relevant articles obtained through searching the MEDLINE database (from 1966 to January 2005) using the search terms: 'Dairy products', defined as 'raw and processed or manufactured milk, and milk-derived products' including butter, cheese, ice cream, margarine, and milk and cultured milk products (yoghurt). Weinsier and Krumdieck (2000) reviewed 12 articles. Among the 12 articles, six found no effect between intake of dairy products and bone health, five found a positive effect and one found a negative	Cumming and Nevitt (1997) found fourteen studies that evaluated Ca supplements (four randomized trials, three non-randomized trials and seven observational epidemiological studies) and 23 observational studies that evaluated dietary Ca (non-randomized trials). Main conclusion emphasized by authors was that ↑ Ca intake among postmenopausal women appeared to be associated with a small ↓ in risk of fracture, with ~30% ↓ in fracture risk among those taking higher amounts of Ca (1g daily as a supplement). Authors concluded that there is weak evidence of a protective capacity of dairy products on bone health.

		effect. Women <30 years seemed to gain the most benefit.	
Budek AZ, Hoppe C et al, 2007 Study Design: Non-Randomized Controlled Trial Class: C Rating:	N=24 males, aged eight years. N=12 per group. Location: Denmark.	Interventions per day for seven days: 1) 1.5L skimmed milk 2) 250g low-fat meat. Each added 53g of PRO to the diet. Serum bone-specific alkaline phosphate (s-BAP), serum C-terminal telopeptides of type I collagen (s-CTX), and serum osteocalcin (s-OC) were measured at baseline and on day seven.	s-OC (P<0.003) and s-CTX (P<0.04) were significantly ↓ in milk group compared to meat group. s-BAP ↓ in both groups, but there were NS differences between groups Boys in milk group ↑ body weight by 0.54kg compared with the boys in meat group, that did not exhibit a Δ body weight (P=0.003).
Huncharek M, Muscat J et al, 2008 Study Design: Meta-analysis or Systematic Review Class: M Rating:	N=21 studies with 3,821 subjects (83% female). Age: Four to 17.3 years.	Search terms used: Bone/bones, dairy products, Ca and Ca/dietary to identify relevant studies published between 1966 and 2006. Data were pooled from RCTs and observational studies using the primary outcomes of summary mean difference bone mineral content (BMC).	Combining data from 21 RCTs using total body bone mineral content (TB-BMC) as the outcome of interest, yielded a non-statistically significant ↑ in BMC of 2g (supplemented vs. controls). Sensitivity tests revealed that baseline Ca intake could be accounting for statistical heterogeneity. When results from three studies utilizing ↓ intake subjects were pooled, ↑ dairy/Ca intake was significantly associated with a mean BMC ↑ of 49g. Pooling data from two studies combining dairy/Ca and vitamin D

			supplementation showed a significant mean ↑ in lumbar spine BMC of 35g.
Kanis JA, Johansson H et al, 2005 Study Design: Meta-analysis Class: M Rating: 	Data from 39,563 adults participating in six prospective cohort studies in Europe, Australia and Canada. Age range: 21-103 years.	Quantified fracture risk associated with a ↓ dietary intake of milk and Ca and to explore dependence of this risk with age, sex and BMD.	NS relationship between ↓ intake of Ca and hip fracture risk in either sex at any age. For osteoporotic fractures, a small, but significant risk was found from the age of 80 years (RR=1.15; 95% CI: 1.02-1.30); however association was no longer significant when adjusted for BMD. Weak, but significant correlation between intake of milk and BMD (r=0.03643, P=4.5 x 10-10).
Konstantynowicz et al 2007 Study Design: Case-Control Study Class: C Rating: 	N=91 cases with fractures (57 boys and 34 girls, aged 2.5-20 years) and 273 age- and sex-matched controls without fractures (three per case, 171 boys and 102 girls). Location: Poland.	Examined association between consumption of a milk-free diet and fracture risk. All children with cow's milk allergy were treated with a restrictive milk-free diet for 2.5 to 14 years. Weight, height, BMD and body composition were measured in all children, while Ca intake was assessed through 24-hour recall in a sub-set of 46 children.	In girls, 29.4% of cases and 11.8% of controls had consumed a milk-free diet, producing an OR for fracture associated with a milk-free diet of 4.6 (95% CI: 1.4, 15.5, P<0.01), while in boys, 23% of cases and 19% of controls had consumed a milk-free diet, producing an OR for fracture associated with a milk-free diet of 1.3 (95% CI: 0.6, 2.7, NS). No association found between Ca intake, BMD or fracture prevalence in the subset of children, leading authors to conclude that cow's milk allergy was associated with ↑ fracture risk in girls.

Kristensen et al 2005 Study Design: Randomized Crossover Trial Class: A Rating:	11 Caucasian males enrolled and completed the study. Age: 22-29 years Location: Denmark.	Investigated the short-term effects of replacing milk with cola beverages in young men on a low-Ca diet in order to study effect on Ca homeostasis and bone turnover. 2.5L of either cola or semi-skimmed milk were consumed each day in two 10-day experimental periods separated by a 10-day washout period. During the two diet periods, same low-Ca diet was given to the subjects; all meals provided.	An ↑ in serum phosphate ($P<0.001$), 1,25(OH)2D ($P<0.001$), PTH ($P=0.046$) and osteocalcin ($P<0.001$) was observed in the cola period compared to milk period and bone resorption was significantly ↑ following the cola period, seen as ↑ serum CTX ($P<0.001$) and urinary NTX ($P<0.001$) compared to milk period. No Δ observed in serum concentrations of Ca or B-ALP. Authors concluded that the trend towards replacement of milk with cola and other soft drinks results in a low Ca intake, which may negatively affect bone health.
McCabe LD, Martin BR et al, 2004 Study Design: Cross-Sectional Study Class: D Rating:	N=289 white women and 116 white men who participated in the RCT. Their data were combined with data from 265 black women and 75 black men for the cross-sectional study. Age: All subjects ≥60 years of age. Location: United States.	Study examined: 1) Cross-sectional relationship between consumption of Ca and other nutrients from dairy products and BMD at the hip in elderly black and white men and women 2) Impact of Ca supplement intake on the BMD loss in a longitudinal study of white men and women. For the trial, subjects received daily placebo, 750mg Ca per day, or 15mcg 25-hydroxyvitamin D	For all participants, average total Ca intake from dairy was 436±289mg, with an additional 239±93mg coming from nondairy dietary sources. In the cross-sectional analysis, a partial positive correlation was found between total hip BMD and dairy Ca in men ($P<0.05$, $r=0.23$), but not in women (NS, $r=0.02$). Results of the RCT showed that effect of calcium supplementation on femoral neck BMD depended on baseline dietary Ca intake ($P<0.05$).

		per day for four years. For all subjects, dietary intake data was collected using the National Cancer Institute's Health Habits and History questionnaire and BMD was assessed using DEXA.	Participants with deficient diets (<1.5 servings or <450mg Ca per day) at baseline who were treated with Ca had less Δ in femoral neck BMD compared to those treated with placebo. Effect of Ca supplementation on femoral neck and hip BMD was evident in those that were <72 years old (P<0.05) at baseline, but not in those that were >72 years at baseline (NS).
Rockell et al 2005 Study Design: Longitudinal Study Class: C Rating:	N=50 Caucasian children (aged three to 10 years) at baseline. N=28 girls and 18 boys (mean age 8.1±2.0 years) completed follow-up study. Location: New Zealand.	Longitudinal study assessing two-year Δ in bone and body composition in young children with history of prolonged milk avoidance. Ca intake was assessed by FFQ, as well as four-day diet records. BMD and body composition were measured using DEXA.	13 children (28.3%) had history of fracture; five new fractures had occurred during the two-year follow-up. At follow-up, Ca intakes were positively correlated with Z scores for total body bone mineral content (r=0.34, P<0.023), total bone area (r=0.33, P<0.025), ultradistal radial BMD (r=0.36, P<0.014) and 33% radial BMD (r=0.30, P<0.045). Every additional 100mg of Ca consumed was commensurate with a Δ of ~0.1 unit of Z score for these measurements. However, although some catch-up in height had taken place during follow-up, the group remained significantly shorter than reference population, with ↑ BMI. Authors concluded that young milk avoiders

			demonstrated persistent height ↓, overweight and osteopenia at the ultradistal radius and lumbar spine over two years of follow-up.

Research Design and Implementation Rating Summary
For a summary of the Research Design and Implementation Rating results, click here.

Worksheets

Al-Zahrani MS. Increased intake of dairy products is related to lower periodontitis prevalence. *J Periodontol.* 2006; 77 (2): 289-294.

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